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| <b>DECLARATION OF YASUMICHI<br/>HITOSHI UNDER<br/>37 C.F.R. §1.131</b> | Application Number   | 09/843,159     |
|  | Confirmation Number  | 8575           |
|  | Filing Date          | April 25, 2001 |
|  | First Named Inventor | Ying Luo       |
|  | Examiner             | Manjunath Rao  |
|  | Group Art            | 1652           |
|  | Attorney Docket No.  | RIGL-010CIP2   |

This Declaration with the attached Exhibits are being submitted in conjunction with the Applicants' Response to the Office Action dated May 26, 2004.

I, Yasumichi Hitoshi, M.D. Ph.D., do hereby declare as follows.

1. I am currently a program director at Rigel Pharmaceuticals, Inc. (hereinafter "Rigel"), and the work described in the above-referenced patent application was performed with my knowledge.
2. I understand that the claimed subject matter of the above-referenced patent application relates to assays for identifying agents that modulate the poly(A) ribose polymerase activity of Tankyrase H.
3. I have been asked to provide factual evidence relating to the activities of Rigel and Rigel's patent counsel with respect to the claimed subject matter, prior to October 25, 1999 (the filing date of the above-referenced patent application).

4. I have reviewed the Exhibits attached hereto and they all relate to the activities of Rigel or Rigel's patent counsel with respect the claimed subject matter, prior to October 25, 1999.
5. Prior to June 11, 1999, the inventors of the above-referenced patent application identified the sequence of the ADP-ribose polymerase domain of Tankyrase H and identified that Tankyrase H had poly(A) ribose polymerase activity. Evidence for this is provided in Exhibit A. All redacted dates are prior to June 11, 1999.
6. Further, between June 11, 1999, and July 21 1999, the inventors worked towards identifying the full length sequence of Tankyrase H for use in the above-referenced screening assays. Evidence for this is provided in Exhibits B and C. The dates have not been redacted in these exhibits.
7. Finally, between July 20, 1999 and October 25, 1999, the above-referenced patent application was drafted at the law firm of Flehr, Hobach, Test, Albritton and Herbert (hereinafter "Flehr), the law firm contracted to draft the above-referenced patent application. Evidence for this is provided in Exhibits D – H. The dates have not been redacted in these exhibits.
8. Exhibit A consists of a print-out of Tankyrase H amino acid and nucleic acid sequences. On pages, 2, 6 and 7 of this Exhibit, Tankyrase H is identified as having a poly(A) ribose polymerase domain. The date of the print-out was prior to June 11, 1999.
9. Exhibit B consists of a presentation that was made by Xiang Xu, an inventor, that identifies Tankyrase H as having poly(A) ribose polymerase activity on page 3. The date of this presentation was June 15, 1999.
10. Exhibit C consists of signed laboratory notebook pages from Simon Yu, a colleague at Rigel Pharmaceuticals, Inc. These notebook pages show results of experiments directed towards identifying the full length sequence of Tankyrase H for use in the above-

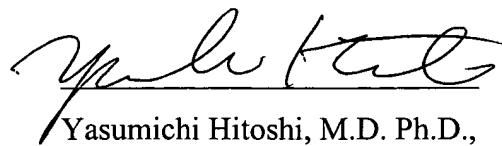
referenced screening assays. The notebook pages are dated July 9, July 13, July 15, July 16 and July 21, 1999, respectively.

11. Exhibit D consists of a letter from Nicole Verona of Rigel to Ms. Robin Silva of Flehr, the law firm contracted to draft the above-referenced patent application. The letter references an invention disclosure (i.e., eight packages of information) for use in preparation of the above-referenced patent application. The date of the letter is July 20, 1999.
12. Exhibit E consists of a letter from Nicole Verona of Rigel to Ms. Robin Silva of Flehr. The letter references diskettes for use in preparation of the above-referenced patent application. The date of the letter is July 22, 1999.
13. Exhibit F consists of a file information page from Flehr, indicating that the file for the above-referenced patent application was opened on July 26, 2003.
14. Exhibit G consists of an e-mail dated August 30, 1999, from Nicole Verona of Rigel to Ms. Dolly Vance of Flehr regarding questions about the above referenced invention disclosure. The body of this e-mail contains text of previous e-mails dated August 20, 1999 and August 26, 1999, also relating to the above referenced invention disclosure.
15. Exhibit H consists of a letter from Nicole Verona of Rigel to Ms. Dolly Vance regarding further documents for use in drafting the above-referenced patent application. The date of the letter is September 30, 1999.
16. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18

of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Respectfully submitted,

Date: 9/3/04



A handwritten signature in black ink, appearing to read "Yasumichi Hitoshi".

Yasumichi Hitoshi, M.D. Ph.D.,

Attachments: Exhibits A - G



final

Exhibit A 09/843,159

in XXII common seen fall from 100

►>3rd Assembly

Longest ORE frame 1 of 1060 amino acids

Longest ORF frame 1 of 1060 amino acids

From amino acid position 84 to 1143

1 MVQTPMLEIIGIILSMKLQLKERL MFALCCYFAVLLQHGAEP TILN T D GRT AL D LAD P S  
61 AKAVLTGEYKKDELLESARSGNEEKMMALLTPLNVNCHASDGRKSTPLHAA GY N RVK IV  
121 QLLQH GADVHAKDKGDLVPLHNACSYGHYEVTELLVKGACVNAMDLWQFTPLHEAASK  
181 NRVEVCSLLL SYGADPTLLNCHNKS AIDLAPTPQLKERL AYE FKGH SLLQAAREADVTRI  
241 KKHL SLEMVNFKHPQTHETALHCAAASPYPKRKQICELLRLKGANINEKTKEFLTPLHVA  
301 SEKAHNDVVVEVVVKHEAKVNALDNLGQTS L HRAAYCGH L QTCRLLS YGCDPNIISLQGF  
361 TALQMGNENVQQLLQEGISLGNSEADRLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQS  
421 TPLHFAAGYNRVSVEYLLQHGADVHAKDKGGLVPLHNACSYGHYEV AELLVKGAVNV  
481 ADLWKFTPLHEAAAGKYEICKLLLQHGADPTKKNRDGNTPLDLVKG DTDIHYLLRGDA  
541 ALLDAAKKGCLARVKKLSSPDNVNCRDTQGRHSTPLHAA GYNNLEVAEYLLQHGADVNA  
601 QDKGGL I PLHNAAS YGHVDVAALLIKYNACVNATDKW AFTPLHEAAQKGR TQLCALLAH  
661 GADPTLK NQEGQTPLD L VSADDVSALLTAAMPPSALPS CYKPQV LNGVRSPGATADALSS  
721 GPSSPSSLSAASSLDNLSGSFSELSSLVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGL  
781 EHLM DIFEREQITLDVL VEMGHKELKEIGINAYGHRHKLIGV ER L ISGQQQLNPYLTLN  
841 TSGSGTILIDLSPDDKEFQSVEEEMQSTVREHRDGGHAGGIFNRYN ILKIQKVCNKKLWE  
901 RYTHRRKEVSEENHNHANERMLFHGSPFVN AIIHKGFD ERHAYIGMFGAGIYFAENSSK  
961 SNQVYVGIGGGTGPVHKDRSCYI CHRQLLFCRVTLGKSFLQFSAMKMAHSPPGHHSTVG  
1021 RPSVNGLALAEYVIYRGEQAYPEYLITYQIMRPEGMVDGZ

1 GAAGTGCAGGGGGTGGATTTCCTGGAATTGCCTTAGTAGTACCAACCAAGGCACGT  
61 CTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTATCATTAAGGTTGGC  
121 GGAAAGACGTAGTTGAATATTCGTTCAAGATGGTCAAATGTCAAGCACGTGATGATG  
181 GGGGCCTTATTCTCTTCATAATGCATGCTTTGGCATGCTGAAGTAGTCATCTCC  
241 TTTTGCAGACATGGTGCAGACCCAAATGCTCAGAGATAATTGGATTACTCCTCTCC  
301 AAGCTGCAATTAAAGGAAAGATTGATGTTGCATTGTTGCTATTGAGCTGTTA  
361 CAGCATGGAGCTGAGCCAACCACCTAAATACAGATGGAAGGACAGCATTGGATTAGCA  
421 GATCCATCTGCCAAGCAGTCTACTGGTAATATAAGAAAGATGAACTCTTAGAAAGT  
481 GCCAGGAGTGGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAATGTCACAGTC  
541 CACGCAAGTGTGGCAGAAAGTCACCTCATTACATTGGCAGCAGGATATAACAGAGTA  
601 AAGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCATGCTAAAGATAAAGGTGAT  
661 CTGGTACCATACACAAATGCCCTTATGGCATTATGAAAGTAACCTGAACTTTGGTC  
721 AAGCATGGTGCCTGTGAAATGCAATGGACTTGTGGCAATTCACTCCTCTTCATGAGGCA  
781 GCTCTAAAGAACAGGGTTGAAGTATGTTCTCTCTTAAGTTATGGTGCAGACCCAACA  
841 CTGCTCAATTGTCACAAATAAAAGTGTATAGACTGGCTCCCACACCACAGTTAAAGAA  
901 AGATTAGCATATGAATTAAAGGCCACTGTTGCTGCAAGCTGCACGAGAAAGCTGATGTT  
961 ACTCGAATCAAAAAACATCTCTCTGGAAATGGTAATTCAAGCATCCTCAAACACAT  
1021 GAAACAGCATTGCATTGTGCTGTCATCTCCATATCCAAAAGAAAGCAAATATGTGAA  
1081 CTGTTGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTGACTCCTCTG  
1141 CACGTGGCATCTGAGAAAAGCTCATATGATGTTGTAAGTAGTGGTAAACATGAAGCA  
1201 AAGGTTAATGCTCTGGATAATCTGGTCAAGACTCTCTACACAGAGCTGCATATTGTTGGT  
1261 CATCTACAAACCTGCCGCCTACTCCTGAGCTATGGGTGATCCTAACATTATCCCTT  
1321 CAGGGCTTACTGCTTACAGATGGAAATGAAAATGTACAGCAACTCCTCAAGAGGGT  
1381 ATCTCATTAGGTAATTCAAGAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGAT  
1441 GTCGAAACTGTAAAAAAACTGTGTAAGTGTCAACTGCAAGAGACATTGAAGGG  
1501 CGTCAGTCTACACCACCTCATTGCAAGCTGGGTATAACAGAGTGTCCGGTGGAAATAT  
1561 CTGCTACAGCATGGAGCTGATGTCATGCTAAAGATAAAGGAGGCCCTGTACCTTGAC  
1621 AATGCATGTTCTTATGGACATTATGAAGTTGCAAGACTCTGTTAAACATGGAGCAGTA  
1681 GTTAATGTAAGCTGATTATGGAAATTACACCTTACATGAAGCAGCAGCAAAGGAAAA  
1741 TATGAAATTGCAAACCTCTGCTCCAGCAGGGTGCAGACCCCTACCAAAAAACAGGGAT  
1801 GGAAATACTCCTTGGATCTGTTAAAGATGGAGATACAGATATTCAATTCTGCTTAGG  
1861 GGAGATGCAGCTTGCAGATGCTGCCAAGAAGGGTTGTTAGCCAGAGTGAAGAAGTTG  
1921 TCTTCTCCTGATAATGTAATTGCCCGATACCCAAGGCAGACATTCAACACCTTACAT

1981 TTAGCAGCTGGTTATAATAATTAGAAGTTGCAGAGTATTGTTACAACACGGAGCTGAT  
 2041 GTGAATGCCAAGACAAAGGAGGACTTATTCCCTTACATAATGCAGCATCTTACGGGCAT  
 2101 GTAGATGTAGCAGCTACTAATAAAAGTATAATGCATGTCAATGCCACGGACAAATGG  
 2161 GCTTCACACCTTGCACGAAGCAGCCAAAAGGGACGAACACAGCTTGTGCTTGTG  
 2221 CTAGCCCATGGAGCTGACCGACTCTTAAACAGGAAGGACAAACACCTTAGATTTA  
 2281 GTTTCAGCGGATGATGTCAGCGCTCTGACAGCAGCCATGCCCATCTGCTCTGCC  
 2341 TCTTGTACAAGCCTCAAGTGCTCAATGGTGTGAGAAGGCCAGGAGCCACTGCAGATGCT  
 2401 CTCTCTTCAGGCCATCTAGCCATCAAGCCTTCTGCAGCCAGCAGTCTGACAACCTTA  
 2461 TCTGGGAGTTTCAGAACTGTCTCATTAGTTAGTTCAAGTGGAACAGAGGGTGTCTCC  
 2521 AGTTGGAGAAAAGGAGGTTCCAGGAGTAGATTTAGCATAACTCAATTGTAAGGAAT  
 2581 CTTGGACTTGACCACTAATGGATATATTGAGAGAGAACAGATCAGTTGGATGTATTA  
 2641 GTTGAGATGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGGACATAGGCAC  
 2701 AAACATAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTAACCCATATT  
 2761 ACTTTGAACACCTCTGGTAGTGGAACATTCTTATAGATCTGTCCTGATGATAAAGAG  
 2821 TTTCAGTCTGGAGGAAGAGATGCAAAGTACAGTTGAGAGCACAGAGATGGAGGTCAT  
 2881 GCAGGTGGAATCTCAACAGATAACATATTCTCAAGATTCAAAGGTTGTAAACAAGAAA  
 2941 CTATGGAAAGATACTACCCGGAGAAAAGAAGTTCTGAAGAAAACCACAACCATGCC  
 3001 AATGAACGAATGCTATTTCATGGGTCCTTTGTGAATGCAATTATCCACAAAGGCTT  
 3061 GATGAAAGGCATGCGTACATAGGTGGTATTTGGAGCTGGCATTATTTGCTGAAAC  
 3121 TCTTCAAAAGCAATCAATATGTATATGAAATTGGAGGAGGTACTGGGTGTCCAGTTCA  
 3181 AAAGACAGATCTGTTACATTGCCACAGGCAGCTGCTTTGCCGGTAACCTTGGGA  
 3241 AAGTCTTCCTGCAGTTCAGTGCAATGAAATGGCACATTCTCCTCAGGTCACTCA  
 3301 GTCACTGGTAGGCCAGTGTAAATGCCCTAGCATAGCTGAATATGTTATTACAGAGGA  
 3361 GAACAGGCTTATCCTGAGTATTTAATTACTTACAGATTGAGGCCTGAAGGTATGGTC  
 3421 GATGGATAAAATAGTTATTAAAGAAACTAATTCCACTGAACCTAAATCATCAAAGCAGC  
 3481 AGTGGCCTTACGTTTACTCCTTGCTGAAAAAA

ref|NP\_003738.1|PTNKS| TANKYRASE >gi|3929219 (AF082556) TRF1-interacting ankyrin-related

ADP-ribose polymerase [Homo sapiens] Length = 1327  
 Score = 1640 bits (4199), Expect = 0.0  
 Identities = 790/1023 (77%), Positives = 871/1023 (84%), Gaps = 11/1023 (1%)  
 Query: 35 VLLQHGAEPILNTDGRITALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLN 94  
 VLLQHGA+P I NTDG++ALDLADPSAKAVLTGEYKKDELLE+ARSGNEEK+MALLTPLN  
 Sbjct: 300 VLLQHGADPNIRNTDGKSALDLADPSAKAVLTGEYKKDELLEAARSGNEEKLMMALLTPLN 359  
 Query: 95 VNCHASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVTE 154  
 VNCHASDGRKSTPLHLAAGYNRV+IVQLLQHGADVHAKDKG LVPLHNACSYGHYEVTE  
 Sbjct: 360 VNCHASDGRKSTPLHLAAGYNRVIVQLLQHGADVHAKDKGLVPLHNACSYGHYEVTE 419  
 Query: 155 LLVKHGACVNAMDLWQFTPPLHEAASKNRVEVCSSLSSYGADPTLLNCHNKSAILDAPTPQ 214  
 LL+KHGACVNAMDLWQFTPPLHEAASKNRVEVCSSLSS+GADPTL+NCH KSA+D+APTP+  
 Sbjct: 420 LLLKHGACVNAMDLWQFTPPLHEAASKNRVEVCSSLSSHGADPTLVNCHGKSAVDMAPTP 479  
 Query: 215 LKERLAYEFKGHSLLQAAREADVTRIKKHLSEMVNFKHPQTHETALHCAAASPYPKRKQ 274  
 L+ERL YEFKGHSLLQAAREAD+ ++KK L+LE++NFK PQ+HETALHCA AS +PKRKQ  
 Sbjct: 480 LRERLTYEFKGHSLLQAAREADLAKVKKTLALEIINFQQPQSHETALHCAVASLHPKRQ 539  
 Query: 275 ICELLRKGANINEKTKFLTPLHVAXXXXXXXXXXXXXXXLDNLGQTS LHRAA 334  
 + ELLLRKGAN+NEK K+F+TPLHVA+ LD LGQT+LHRAA  
 Sbjct: 540 VTELLLRKGANVNEKNKDFMTPLHVAAERAHNDVMEVLHKHGAKMNALDTLGQTALHRAA 599  
 Query: 335 YCGHILQTCRLLLSYGCDPNIISLQGFTALQMGNENVQQLLQEGISLGNSEADRQLEAAK 394  
 GHLQTCRLLLSYG DP+IISLQGFTA QMGNE VQQ+L E + S+ D +LLEA+K  
 Sbjct: 600 LAGHILQTCRLLLSYGSDFPSIISLQGFTAAQMGNEAVQQILSESTPIRTSDVDYRLLEASK 659

Query: 395 AGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVEYLLQHGADVHAKDKGGLV 454  
 AGD+ETVK+LC+ Q+VNCRD+EGR STPLHFAAGYNRVSVEYLL HGADVHAKDKGGLV  
 Sbjct: 660 AGDLETVKQLCSSQNVNCRDLEGRHSTPLHFAAGYNRVSVEYLLHHGADVHAKDKGGLV 719

Query: 455 PLHNACSYGHYVAELLVKHGAVERNADLWKFTPLHEAAAKGKYEICKLLLQHGADPTKK 514  
 PLHNACSYGHYVAELLV+HGA VNVADLWKFTPLHEAAAKGKYEICKLLL+HGADPTKK  
 Sbjct: 720 PLHNACSYGHYVAELLVRHGASVNADLWKFTPLHEAAAKGKYEICKLLLKHGADPTKK 779

Query: 515 NRDGNTPLDLVKDGTDIHYXXXXXXXXXXXXXXRVKKLSSPDNVNCRDTQGRHST 574  
 NRDGNTPLDLVK+GDTDI RV+KL +P+N+NCRDTQGR+ST  
 Sbjct: 780 NRDGNTPLDLVKEGTDIQLLGDAALLDAAKKGCLARVQKLCTPENINCRTQGRNST 839

Query: 575 PLHLAAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAASYGHVDVAALLIKYNACVNAT 634  
 PLHLAAGYNNLEVAEYLL+HGADVNAQDKGGLIPLHNAASYGHVD+AALLIKYN CVNAT  
 Sbjct: 840 PLHLAAGYNNLEVAEYLL+HGADVNAQDKGGLIPLHNAASYGHVDIAALLIKYNTCVNAT 899

Query: 635 DKWAFTPHEAAQKGRQLCALLLAHGADPTLKNGEQTPLDLVSADDVSALLTAAMPPS 694  
 DKWAFTPHEAAQKGRQLCALLLAHGADPT+KNQEGQTPLDL +ADD+ ALL AMPP  
 Sbjct: 900 DKWAFTPHEAAQKGRQLCALLLAHGADPTMKNQEGQTPLDLATADDIRALLIDAMPPE 959

Query: 695 ALPSCYKPQ---VLNGVRSPGATXXXXXXXXXXXXXXXXXXXXXXXXXXXX 751  
 ALP+C+KPQ V + SP +T  
 Sbjct: 960 ALPTCFKPQATVVSASLISPAST-----PSCLSAASSIDNLTGPLAELAVGGASNAG 1011

Query: 752 XXXXXXXXXXXXKEVPGVDFSITQFVRNLGLEHLMDFEREQITLDVLVEMGHKELKEIGIN 811  
 + EV G+D +I+QF+++LGLEHL DIFE EQITLDVL +MGH+ELKEIGIN  
 Sbjct: 1012 DGAAGTERKEGEVAGLDMNISQFLKSLGLEHLRDIFETEQITLDVLADMGEELKEIGIN 1071

Query: 812 AYGHRHKLIKGVVERLISGQQGLNPYLTNLNTSGSGTILIDLSPDDKEFQSVEEEMQSTVRE 871  
 AYGHRHKLIKGVVERL+ GQQG NPYLT + GTIL+DL+P+DKE+QSVEEEMQST+RE  
 Sbjct: 1072 AYGHRHKLIKGVVERLGGQQGTNPYLTFCVNQGTILLDIAPEDKEYQSVEEEMQSTIRE 1131

Query: 872 HRDGGHAGGIFNRYNLIKQKVCNKKLWERYTHRRKEVSEENHNHANERMLFHGSPFVNA 931  
 HRDGG+AGGIFNRYN++IQQV NKKL ER+ HR+KEVSEENHNH NERMLFHGSPF+NA  
 Sbjct: 1132 HRDGGNAGGIFNRYNVIRIQQVNNKKLRERFCHRQKEVSEENHNHHNERMLFHGSPFINA 1191

Query: 932 IIHKGFDERHAYIGGMFGAGIYFAENSSKSQNQVYVGIGGGTGPVHKDRSCYICHROQLF 991  
 IIHKGFDERHAYIGGMFGAGIYFAENSSKSQNQVYVGIGGGTGPVHKDRSCYICHROQ+LF  
 Sbjct: 1192 IIHKGFDERHAYIGGMFGAGIYFAENSSKSQNQVYVGIGGGTGPVHKDRSCYICHROMLF 1251

Query: 992 CRVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAEYVIYRGEQAYPEYLITYQIM 1051  
 CRVTLGKSFLQFS MKMAH+PPGHHHSV GRPSVNGLA AEYVIYRGEQAYPEYLITYQIM  
 Sbjct: 1252 CRVTLGKSFLQFSTMKMAHAPPGHHSVIGRPSVNGLAYAEYVIYRGEQAYPEYLITYQIM 1311

Query: 1052 RPE 1054  
 +PE  
 Sbjct: 1312 KPE 1314

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GAAGTGCAGCGGGTGGATTCTGGAATTGCCCTAGTAGTAGTACCAACCAAGGCACTG  
 CTTAGGTACACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTATCATTAAGGTTTGGG  
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121 GCAAAGCAGTCTTACTGGTGAATATAAGAAAGATGAACCTCTAGAAAGTGCCAGGAGT  
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661 AAAAAACATCTCTCTGGAAATGGTAATTCAAGCATCCTAAACACATGAAACAGCA  
721 TTGCAATTGTCGCTGCATCTCCATATCCCCAAAAGAAAGCAAATATGTGAACTGTTGCTA  
781 AGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTGACTCCTCTGCACGTTGCA  
841 TCTGAGAAAGCTCATAATGATGTTGTAAGTAGTGGGAAACATGAAAGCAAAGGTTAAT  
901 GCTCTGGATAATCTTGTCAAGACTCTACACAGAGCTGCATATTGTGGTCATCTACAA  
961 ACCTGCCGCTACTCTGAGCTATGGGTGTGATCTAACATTATATCCCTCAGGGCTT  
1021 ACTGCTTTACAGATGGAAATGAAAATGTACAGCAACTCCTCAAGAGGGTATCTCATT  
1081 GTAAATTCAAGAGGCAGACAGACAATTGTGGAAGCTGCAAAGGGTGGAGATGTCGAAACT  
1141 GTAAAAAAACTGTGTACTGTTCAAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCT  
1201 ACACCACTTCATTGCACTGGGTATAACAGAGTGCCGTGGATATCTGCTACAG  
1261 CATGGAGCTGATGTCATGCTAAAGATAAAGGAGGCCATTGACCTTGCACAATGCATGT  
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1501 CCTTTGGATCTTGTAAAGATGGAGATAACAGATATTCAATTATCTGCTTAGGGAGATGCA  
1561 GCTTGCTAGATGTCGCAAGAAGGGTTGTTAGCCAGAGTGAAGAAGTTGCTCTCCT  
1621 GATAATGTAATTGCGCGATAACCAAGGCAGACATCAACACCTTACATTAGCAGCT  
1681 GTTATAATAATTAGAAGTTGCAAGAGTATTGTTACAACACGGAGCTGATGTGAATGCC  
1741 CAAGACAAAGGAGGACTTATTCTTACATAATGCAGCATCTACGGCATGTAGATGTA  
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1861 CCTTGACGAAAGCAGCCAAAAGGGACGAACACAGCTTGTGTTGCTAGCCAT  
1921 GGAGCTGACCCGACTCTAAAAATCAGGAAGGACAACACCTTAGATTTAGTTAGCTCAGCG  
1981 GATGATGTCAGCGCTTCTGACAGCAGCCATGCCCATCTGCTCTGCCCTTGTAC  
2041 AAGCTCAAGTGTCAATGGTGTGAGAAGGCCAGGAGCCACTGCAGATGCTCTCTCA  
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2341 GGGCACAAGGAGCTGAAGGAGATTGAATCAATGCTATGGACATAGGCACAAACTAATT  
2401 AAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTAACCATATTTAACCTTGAAC  
2461 ACCTCTGGTAGTGGAAACAATTCTTATAGATCT  
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ACGAATGCTATTTCATGGGCTCCTTGTGAATGCAATTATCCACAAAGGCTTGATG  
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CAGGCTTATCCTGAGTATTTAATTACTTACCAAGATTATGAGGCCAGGATGGTGC  
ATGGATAAAATAGTATTGAAACTAATTCCACTGAACCTAAACATCAAAGCAGC  
AGTGGCCTCTACGTTTACTCCTTGTGAAAAAA

1 GGCACGAGCTGCAACGAAATGGAAAGATTGATGTTGCATTGTGTTACAGCATGGA  
61 GCTGAGCCAACCR10ATCCTAAATACAGATGGAAGGCAGCATTGGR9ATTTAGCAGATCCATCT  
121 GCCAAAGCAGTGR8CTTACTGGTGAATATAAGAAAGATGAACCTCTAGAAAGTGCCAGGAGT

181 GGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAAATGTCAACTGCCACGCAAGT  
241 GATGGCAGAAAGTCACACTCCATTACATTGGCAGCAGGATATAACAGAGTAAAGAGATTGTA  
301 CAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCA  
361 TTACACAATGCCATTATGGCATTATGAAGTAACGTAACTTGTGCAAGCATGGTACCA  
421 GCCTGTGTAATGCAATGGACTTGTGCAATTCACTCCTCTCATGAGGCAGCTTCAAG  
481 AACAGGGTTGAAGTATGTTCTCTTAAGTTATGGTGCAGACCCAAACACTGCTCAAT  
541 TGTCACAATAAAAGTGTATAGACTTGGCTCCACACCACAGTTAAAGAAAGATTAGCA  
601 TATGAATTAAAGGCCACTCGTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCGAATC  
661 AAAAAACATCTCTCTGGAAATGGTAATTCAAGCATCCTCAAACACATGAAACAGCA  
721 TTGCATTGTGCTGCATCTCCATATCCAAAAGAAAGCAAATATGTGAACTGTTGCTA  
781 AGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTGACTCCTCTGCACGTGGCA  
841 TCTGAGAAAGCTCATATGATGTTGAAAGTAGTGTGAAACATGAAGCAAAGGTTAAT  
901 GCTCTGGATAATCTGGTCAGACTTCTACACAGAGTCATATTGTGGTCATCTACAA  
961 ACCTGCCGCCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCCTCAGGGCTT  
1021 ACTGCTTACAGATGGAAATGAAAATGTACAGCAACTCCTCAAGAGGGTATCTCATTA  
1081 GGTATTTCAGAGGCAGACAGACAATTGCTGAAAGCTGCAAAGGCTGGAGATGTCGAAACT  
1141 GTAAAAAAACTGTTACTGTTAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCT  
1201 ACACCACTTCATTTGAGCTGGTATAACAGAGTGTCCGGTGGAAATATCTGCTACAG  
1261 CATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGGCTTGTACCTTGCACAATGCATGT  
1321 TCTTATGGACATTATGAAGTTGCAAGACTTCTGTTAAACATGGAGCAGTAGTTAATGTA  
1381 GCTGATTTATGAAATTACACCTTACATGAAGCAGCAGCAAAGGAAAATATGAAATT  
1441 TGCAAACCTCTGCTCCAGCATGGCAGACCCCTACCAAAAAAAACAGGGATGAAATACT  
1501 CCTTGGATCTGTTAAAGATGGAGATACAGATATTCAATTCTGCTTAGGGAGATGCA  
1561 GCTTGCTAGATGCTGCCAGAAGGGTTGTTAGCCAGAGTGAAGAAGTTGCTTCTCCT  
1621 GATAATGTAATTGCCCGATAACCAAGGCAGACATTCAACACCTTACATTAGCAGCT  
1681 GGTATAATAATTAGAAGTTGAGCTTACAACACGGAGCTGATGTAATGCC  
1741 CAAGACAAAGGAGGACTTATTCTTACATAATGCAGCATCTACGGGATGTAGATGTA  
1801 GCAGCTCTACTAATAAGTATAATGCATGTCATGCCACGGACAAATGGCTTCA  
1861 CCTTGACGAAGCAGCCAAAAGGGACGAACACAGCTTGTGCTTGTCTAGCCAT  
1921 GGAGCTGACCCGACTCTAAAAATCAGGAAGGACAAACACCTTGTAGATTAGTTAGCTCAGCG  
1981 GATGATGTCAGCGCTTCTGACAGCAGCCATGCCCATCTGCTCTGCCCTTGTAC  
2041 AAGCTCAAGTGTCAATTGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTTCA  
2101 GGTCCATCTAGCCCATCAAGCCTTCTGACAGCAGCCACTGCAGATGCTCTCTTCA  
2161 TTTTCAGAACTGCTTCAATTAGTTAGTCAGTGGAAACAGAGGGTGTCCAGTTGGAG  
2221 AAAAAGGAGGTTCCAGGAGTAGATTTCAGATAACTCAATTGTAAGGAATCTGGACTT  
2281 GAGCACCTAATGGATATATTGAGAGAGAACAGATCACTTGGATGTTAGTTGAGATG  
2341 GGGCACAAGGAGCTGAAGGAGATTGAAATCAATGCTTATGGACATAGGCACAAACTAATT  
2401 AAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGCTTAACCCATATTAACTTGAAC  
2461 ACCTCTGGTAGTGGAAACAATTCTTATAGF5ATCTGCTCTGTGATAAAGAGTTCACTGCTF6  
2521 GTGGAGGAAGAGATGCAAAGTACAGTTGAGAGCACAGAGAF7TGGAGGTGTGAGGTGGA  
2581 ATCTCAACAGATAACATTCTCAAGATTCAAGAGTTGTAACA  
Plus  
3' end

GTCTCCTGATGATAAAGAGTTCACTGTTGAGGAAGAGATGCAAAGT  
ACAGTTGAGAGCACAGAGATGGAGGTATGCAGGTGGAATCTTC  
AACAGATAACATATTCTCAAGATTCAAGGTTGTAACAAGAAACTATGGGA  
AAGATACACTCACCGGAGAAAGAAGTTCTGAAGAAAACCACAACCATGCCAATGA  
ACGAATGCTATTCTGGTCTCTTGTGAATGCAATTATCCACAAAGGTTGATG  
AAAGGCATGCGTACATAGGTGGTATGTTGAGCTGGCATTATTTGCTGAAACTCTT  
CCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCCAGTTCAACAAAG  
ACAGATCTGTTACATTGCCACAGGCAGCTGCTTTGCCGGTAACCTGGGAAAG  
TCTTCTGCAAGTCAGTGAATGAAATGGCACATTCTCCTCCAGGTATCACTCAGTC  
ACTGGTAGGCCAGTGAAATGGCTAGCATTAGCTGAATATGTTATTACAGAGGAGAA  
CAGGCTTATCCTGAGTATTAAATTACTTACAGATTATGAGGCTGAAGGTATGGTCG  
ATGGATAAAATAGTTATTAAAGAAACTAATTCAACTGAACCTAAACATCAAAGCAGC  
AGTGGCCTCTACGTTTACTCCTTGCTGAAAAAA

gi|3929219 (AF082556) TRF1-interacting ankyrin-related ADP-ribose polymerase  
 [Homo sapiens] Length = 1327  
 Score = 464 bits (1181), Expect = e-130  
 Identities = 223/309 (72%), Positives = 249/309 (80%) Frame = +2  
 Query: 2 LEMVNFKHPQTETALHCAAASPYPKRKQICELLRLKGANINEKTFELTPLHVASXXXX 181  
 LE++NFK PQ+HETALHCA AS +PKRKQ+ ELLLRKGAN+NEK K+F+TPLHVA+  
 Sbjct: 511 LEIINFQPKQSHETALHCAVASLHPKRKVTELLLRKGANVNEKNKDFMTPLHVAAERAH 570  
 Query: 182 XXXXXXXXXXXXXXXXXLDNLGQTSLHRAAYCGHLQTCRLLSYGCDPNIISLQGFTALQM 361  
 LD LGQT+LHRAA GHLQTCRLLSYG DP+IISLQGFTA QM  
 Sbjct: 571 NDVMEVLHKHGAKMNALDTLGQTALHRAALAGHLQTCRLLSYGSDPSIISLQGFTAAQM 630  
 Query: 362 GNENVQQLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHF 541  
 GNE VQQ+L E + S+ D +LLEA+KAGD+ETVK+LC+ Q+VNCRD+EGR STPLHF  
 Sbjct: 631 GNEAVQQILSESTPIRTSDVDYRLLEASKAGDLETVKQLCSSQNVNCRDLEGRHSTPLHF 690  
 Query: 542 AAGYNRVSVVEYLLQHGADVHAKDKGGLVPLHNACSYGHYEVAELLVKGAVVNVALWK 721  
 AAGYNRVSVVEYLL HGADVHAKDKGGLVPLHNACSYGHYEVAELLV+HGA VNVALWK  
 Sbjct: 691 AAGYNRVSVVEYLLHHGADVHAKDKGGLVPLHNACSYGHYEVAELLVRHGASVNVALWK 750  
 Query: 722 FTPLHEAAAKGKYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDTXIQXXXXXXXXX 901  
 FTPLHEAAAKGKYEICKLLL+HGADPTKKNRDGNTPLDLVK+GDT IQ  
 Sbjct: 751 FTPLHEAAAKGKYEICKLLLKGADPTKKNRDGNTPLDLVKEGDTDIQDLLKGDAALLDA 810  
 Query: 902 XXKGCFXQI 928  
 KGC ++  
 Sbjct: 811 AKKGCLARV 819

Longest ORF frame 2 of 310 amino acids

From amino acid position 1 to 311

1 LEMVNFKHPQTETALHCAAASPYPKRKQICELLRLKGANINEKTFELTPLHVASEKAH  
 61 NDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGHLQTCRLLSYGCDPNIISLQGFTALQM  
 121 GNENVQQLLQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHF  
 181 AAGYNRVSVVEYLLQHGADVHAKDKGGLVPLHNACSYGHYEVAELLVKGAVVNVALWK  
 241 FTPLHEAAAKGKYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDTXIQDLLRGDAXXLD  
 301 AXKGCFXQIX

1 GCTGGAAATGGTGAATTCAAGCATCCTCAAAR7CACATGAAACAGCATTGCATTGTGCTGC  
 61 TGCATCTCCATATCCAAAAGAAAGCAA6TATGTGAACTGTTGCTAAGAAAAGGAGCAA  
 121 R5CATCAATGAAAAGACTAAAGAATTCTGACTCCTCTGCACGTGGCATCTGAGAAAAGCTCA  
 181 TAATGATGTTGTTGAAAGTAGTGGTAAACATGAAGCAAAGGTTAATGCTCTGGATAATCT  
 241 TGGTCAGACTTCTACACAGAGCTGCATATTGTTGCTCATCTACAAACCTGCCGCTACT  
 301 CCTGAGCTATGGGTGTGATCCTAACATTATATCCTTCAGGGCTTACTGCTTACAGAT  
 361 GGGAAATGAAAATGTACAGCAACTCCTCAAGAGGGTATCTCATTAGGTAATTAGGAC  
 421 AGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAAACTGTAAAAAAACTGTG  
 481 TACTGTTCAGAGTGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCACTTCATT  
 541 TGCAGCTGGTATAACAGAGTGTCCGTGGTGAATATCTGCTACAGCATGGAGCTGATGT  
 601 GCATGCTAAAGATAAAGGAGGCCTTGTACCTTGCAACATGCATGTTATGGACATTA  
 661 TGAAGTTGAGAACTTCTGTTAACATGGAGCAGTAGTTAATGTTAGCTGATTTATGGAA  
 721 ATTTACACCTTACATGAAGCAGCAGCAAAGGAAATATGAAATTGCAAACCTCTGCT  
 781 CCAGCATGGTGCAGACCCCTACCAAAAAAAACAGGGATGGAATACTCCTTGGATCTGT  
 841 TAAAGATGGAGATACANATATTCAAGATCTGCTTAGGGAGATGCANNTTNCTAGATGC  
 901 TGCCNANAAGGGTTTTTANCCAGATTNA

>EST assembled

Good protein homology to

gi|3929221 (AF082557) TRF1-interacting ankyrin-related  
ADP-ribose polymerase [Homo sapiens]

TITLE Tankyrase, a poly(ADP-ribose) polymerase at human telomeres  
JOURNAL Science 282, 1484-1487 (1998)

Longest ORF frame 3 of 258 amino acids

HVASEKAHNDVVEVVVKHEAKVNALDNLGQTSRHLQTCRLLLSYGCDPNIISL  
QGFTALQMGNENVQQLLQEGISLGNSEADROLLEAAKAGDVETVKKLCTVQSVNCRDIEG  
RQSTPLHFAAGYNRVSVEYLLQHGADVAKDKGGLVPLHNACSYGHYEVAELLVKHGAV  
VNVAIDLWKFPLHEAAAKGKYEICKLLLQHGADPTKKNRDGNTPLDLVKDGDXTIQDLLR  
GDAXXLDAAXKGCFXQIX

TGCACGTGGCATCTGAGAAAGCTCATAATGATGTTGTAAGTAGTGGTAAACATGAAG  
R2CAAAGGTTAATGCTCTGGATAATCTGGTCAGACTCTCTACACAGAGCTGCATNTTGTG  
GNCATCTACAAACCR1TGCGCCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCC  
TTCAGGGCTTACTGCTTACAGATGF4GGAATGAAAATGTACAGCAACTCCTCCAAGAGG  
GTATCTCATTAGGTAATTCAAGGGCAGACAGAR4CAATTGCTGGAAGCTGCAAAGGCTGGAG  
ATGTCGAAACTGTAAAAAAACTGTGTACTGTR3CAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTGCAAGCTGGGTATAACAGAGTGTCCGTGGTGAAT  
ATCTGCTACAGCATGGAGCTGATGTCATGCTAAAGATAAAGGAGGCCCTGTACCTTTGC  
ACAATGCATGTTCTTATGGACATTATGAAGTTGCAAGACTTCTGTTAAACATGGAGCAGF3  
TAGTTAATGTAGCTGATTATGAAATTTACACCTTACATGAAGCAGCAGCAAAGGAA  
AATATGAAATTGCAAACCTCTGCTCCAGCATGGTF1CAGACCCCTACCAAAAAACAGGG  
ATGGAATACTCCTTGGATCTGTTAAAF2AGATGGAGATACANATATTCAAGATCTGCTTA  
GGGGAGATGCANNTTNCTAGATGCTGCCNANAAGGGTTGTTANCCAGATTNA

TGCACGTGGCATCTGAGAAAGCTCATAATGATGTTGTAAGTAGTGGTAAACATGAAG  
CAAAGGTTAATGCTCTGGATAATCTGGTCAGACTCTCTACACAGAGCTGCATNTTGTG  
GNCATCTACAAACCTGCCGCTACTCCTGAGCTATGGGTGTGATCCTAACATTATATCCC  
TTCAGGGCTTACTGCTTACAGATGGAAATGAAAATGTACAGCAACTCCTCCAAGAGG  
GTATCTCATTAGGTAATTCAAGGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAG  
ATGTCGAAACTGTAAAAAAACTGTGTACTGTCAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTGCAAGCTGGGTATAACAGAGTGTCCGTGGTGAAT  
ATCTGCTACACCATGGAGCTGATGTCATGCTAAAGATAAAGGAGGCCCTGTACCTTTGC  
ACAATGCATGTTCTTATGGACATTATGAAGTTGCAAGACTTCTGTTAAACATGGAGCAG  
TAGTTAATGTAGCTGATTATGAAATTTACACCTTACATGAAGCAGCAGCAAAGGAA  
AATATGAAATTGCAAACCTCTGCTCCAGCATGGTCAGACCCCTACCAAAAAACAGGG  
ATGGAATACTCCTTGGATCTGTTAAAGATGGAGATACANATATTCAAGATCTGCTTA  
GGGGAGATGCANNTTNCTAGATGCTGCCNANAAGGGTTGTTANCCAGATTNA

>cip6c1p5F2

TCATTATCTGCTTAGGGGAGATGCAGCTTT  
GCTAGATGCTGCCAAGAAGGGTTGTTAGCCAGAGCGAAGAAGTTGCTTCCTGATAA  
TGTAAATTGCCGCGATAACCAAGCAGACATTCAACACCTTACATTAGCAGCTGGTTA  
TAATAATTAGAAGTTGCAAGAGTATTGTTACAACACGGAGCTGATGTGAATGCCAAGA  
CAAAGGAGGACTTATTCTTACATAATGCAGCATCTACGGCATGTAGATGTAGCAGC  
TCTACTAATAAAAGTATAATGCATGTCATGCCACGGACAAATGGCTTACACCTT  
GCACGAAGCAGCCAAAAGGGACAAACAGCTTGTGCTTAGCCATGGAGC  
TGACCCGACTCTTAAACATCAGGAAGGACAAACACCTTACATTAGTTAGTTCAAGCAGGATGA  
TGTCAAGCGCTCTCTGACAGTAGCCATGCCCATCTGCTCTGCCCTTGTACAAGC  
CTCAAGTGTCAATGGGTGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCCTCAGGT  
CCATCTAGCCCATCAAGCCTTCTGCANCCAGCAGTCTGACAACATTCTGGAGTT

>cip6c2p5-F3

GGATGGAAATACTCCTTGGATCTGTTAAAGATG  
GAGATACAGATATTCAAGATCTGCTTAGGGGAGATGCAGCTTGCTAGATGCTGCCAAGA  
AGGGTTGTTAGCCAGAGTGAAGAAGTTGCTTCTCCTGATAATGTAATTGCCGCGATA  
CCCAAGGCAGACATTCAACACCTTACATTAGCAGCTGGTTATAATAATTAGAAGTTG  
CAGAGTATTGTTACAACACGGAGCTGATGTGAATGCCAAGACAAAGGAGGACTTATT  
CTTACATAATGCAGCATCTACGGCATGTAGATGTAGCAGCTACTAATAAAAGTATA



Exhibit B  
09/843,159

6/15/1999 w/ Tank northern  
blob  
↳ This slide is for Jassey

## Chk1 two-hybrid screening

**Bait: Chk1**

is a protein kinase required for cell cycle arrest in response to DNA damage

**Hit: a novel protein homology to ATP-dependent RNA helicase**  
belongs to the DEAD-box RNA helicase family

The fission yeast *cdc28(+)* encodes a member of the DEAD-box family of putative RNA helicases involved in pre-mRNA splicing and cell cycle progression

a new gene encoding a putative DEAD box helicase have been isolated to suppress uncontrolled mitosis by overexpression *cdc25* in fission yeast  
(Chk1 and 14-3-3 proteins also show up in this screening)

It is interesting to characterize the interaction of Chk1 and the novel RNA helicase and its role in cell cycle control

## Potential targets for further pursuing

|            |                                       |
|------------|---------------------------------------|
| p21 hit:   | Tankyrase homolog                     |
| Traf4 hit: | Cdk liked kinase                      |
| hRad9 hit: | PP5                                   |
| PNCA hits: | a novel helicase                      |
|            | a human homolog of SNM1               |
|            | a novel endo/exo-ribonuclease         |
| Chk1 hit:  | an ATP-dependent RNA helicase homolog |

### Target validation:

- full length cloning
- examine the RNA expression in tumor verse normal tissues
- peptide binding library screening in YTH---->functional assay
- generate dominant-negative mutant

## **p21 hit: a Tankyrase homolog**

**Takyrase (a poly(ADP-ribose) polymerase at human telomeres)**

- a protein with homology to ankyrin and to the catalytic domain of ADP-ribose polymerase (PARP)
- is localized to human telomeres
- binds to the telomeric protein TRF1 (telomeric repeat binding factor-1)
- is a positive regulator of telomere length maintenance

SEP 08 2004 JC 32 Project No. \_\_\_\_\_

124

Book No. \_\_\_\_\_

Exhibit C 09/843,169

TITLE Smart HB for #2 (CIP5)

From Page 1 TRADEMARKS

See pg. 1.

7/9/99 (5)

SS sym.

HB(1)

HB(2)

polymer HB (1μg)  
Smart Oligo II (9040495)

0.5 μg (1)

0.5 μg (1)

Primer  
H2O

5CPS

1x

#2(R14)

2.5

1x

2.5

70°C 3' ice

5x

2.5

5x 1°

2

0.1M-DTT

1

dNTP mix

1

RT

1

10x

4°C 15h

+50 μL Tricine-EDTA buffer, 22°C 7' ice.  
(10 μg/μL)

upm Nup

R11 R14

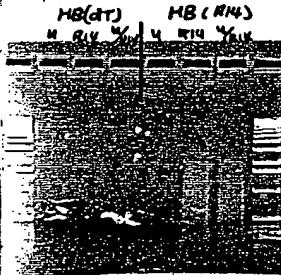
PCR

upm R14 upm  
R11

HB(1)

HB(2)

Cap30



7/12 (1) PCR (2p)

primers: Nup R11 N R11

X C10B11 IP3 HB(1P14) N R11 R11 N R14 R14

HB(1) IP (4 μg R14) 0.5x

HB(2) IP (4 μg R14) 1.0x

Cap23.



1/10

1/10

1/10

↓ GP X

#2-Cap1 (N R11)

#2-Cap2 "

→

To Page No. \_\_\_\_\_

Witnessed &amp; Understood by me,

Date

Invented by

Date

JH

8/28/99

Suz

7/9/99

Recorded by

Suz





**TITLE** \_\_\_\_\_ **PCMA-140 #4.** \_\_\_\_\_ **Book No.** \_\_\_\_\_

Project No. \_\_\_\_\_

**Book No.** \_\_\_\_\_

127.

From Page No. 12

7/12/99 (D) PCR insert screening again (last time the amount clones are not enough, primer mix F5/R8)

mini plant  
prep

BB-FBR7 #9-FBR7  
11 16 17 19 20 | 16 15 20

|             |             |
|-------------|-------------|
| #4-FER.7-11 | 7/3         |
| -19         |             |
| -20         | to sequence |
| #4-FER.7-15 |             |

7/15(4) Clones per insert screening

↓ Muni (7/14)

A photograph showing a row of 10 small, white, cylindrical dental implants standing upright in a dark, rectangular container. The implants are evenly spaced and have a smooth, rounded top.

1b② 7/13/11 insert check result: all of them have <sup>panel</sup> [REDACTED]

To Page No.

Witnessed & Understood by me.

Date \_\_\_\_\_

Invented by

5

Date

7/13/99

Recorded by

Project No. \_\_\_\_\_

128

Book No. \_\_\_\_\_

TITLE CIPS (#2) Marathon

From Page No. 104

7/1/98 (2) Compare pH of PCR Buffer.

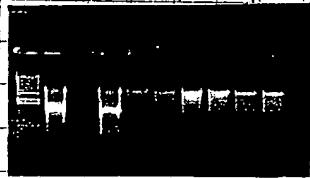
API R14 APV  
R14

Template (HB Marathon) 30ng in 1.5 in 25 μl PCR.

+ 0.5 μl 1M HCl + 0.2 μl 1M APV  
+ 1.5 μl " + 0.5 μl "  
+ 2.1 μl " + 0.8 μl "Capzo  
useful.HCl 0 0.2 0.5 0.8  
API R14 APV API R14

X

Try New buffer &amp; API.

API R14 APV  
R14API R14 APV New Buffer  
API R14 APV API R14

X

To Page No. \_\_\_\_\_

Witnessed &amp; Understood by me,

JH

Date

8/2/99

Invented by

SJD

Date

7/15/98

Recorded by

SJD

7/16/92

(H2-5-1)

(page date)

(charge)

(sequence)

RACE

① { T+B X 6/25, p111 { Both kit X { #2-B4-1 (6kb) X  
 H.Liver/pl. ✓ (R14, R11) { clonelch kit ✓ -3  
 -4

② { HB(CR) ✓ 6/30, p115-7  
 T+B ✓ R14  
 H.Mela X  
 H.Liver/pl. ✓

{ #2-C1-6 (1kb)  
 (HB) -7  
 -12  
 -14  
 #2-C2-1 (0.6kb)  
 (HB) -5 ✓  
 #2-C3-11 (1.6kb)  
 (HB) -12  
 -18

③ { HB/pl ✓ 7/12, p126-7 X HB too small 9kb  
 H.Leuk/pl ✓ R14 15kb → mini & clones  
 4 Zap mix ✓ okas. → but didn't pull F13/R11 clone X  
 H.B/ps ✓ x too more colony plate no to sequence  
 give pcr gp to FG  
 { #2-D3 (H.Liver)  
 { #2-D4 (4 Zap mix)  
 { #2-D5 (H.B/ps)

④ myself X 7/12, p123, 128  
 HB R14 { Normal Buff  
 different pH but  
 C. Newer buffer

⑤ cloned Marathon Ready cDNA, 7/16, p119

{ H.Fetal Brain X  
 H.Fetal Liver X  
 H.Leukocyte X

X primer adaptor problem

3. [REDACTED] 7/19, p144-5.

{ HB, primord T ✓  
 HB, R14 X

7/20 p137

{ #2-CapA1-3 (1.5kb) ✓ isoform 1  
 -11 (0.5kb) ✓ isoform 3

{ #2-CapA2-3 (1kb)  
 -10  
 -12 (1.2kb) ✓ no seq

(class F13/R11 check)

{ #2-CapA1-29 (1.5kb) ✓  
 -33 (1.2kb) ✓  
 -34 (2.2kb) ✓  
 { #2-CapA2-26 (0.8kb)  
 -29 (0.9kb) ✓

Result: got 2 isoform from Smart RACE. \* got isoform from Library method.

But Marathon did work.

7/22 finish it.





RIGEL

Exhibit D 09/843,149

H93  
FLEHR, HOBACH, TEST  
ALBRITTON & HERBERT

1999 JUL 22 AM 9.02

RECEIVED

July 20, 1999

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva  
Flehr, Hobach, Test, Albritton, & Herbert  
4 Embarcadero Center, Suite 3400  
San Francisco, California 94111-4187

*Per RMS - open  
AS utility*

Re: Provisional Patent Applications.

Dear Ms. Silva,

Per Brian Cunningham's request, enclosed with this letter are eight packages of information generated by Dr. Ying Luo in preparation for provisional patent application filings. Each package pertains to a different genetic sequence that Rigel believes may be commercially useful. Each package contains relevant scientific materials, journal references and abstracts of proposed gene functions.

Please file a provisional patent application for each document.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

*Nicole Verona*

Nicole A. Verona  
Rigel Pharmaceuticals, Inc.

Exhibit D E 09/843,141

FLEHR, HOBACH, TEST  
ALBRITTON & HERBERT

1999 JUL 23 AM 10:04

RECEIVED

July 22, 1999

RIGEL, INC.

VIA FEDERAL EXPRESS

Ms. Robin Silva  
Flehr, Hobach, Test, Albritton, & Herbert  
4 Embarcadero Center, Suite 3400  
San Francisco, California 94111-4187

ORIGINAL Diskette in  
P-68287

Re: Provisional Patent Applications.

Dear Ms. Silva,

It was a pleasure to meet you today. I'm sorry that I did not see you leave; I had intended to give you these diskettes before the end of our meeting.

On these diskettes are the documents that we reviewed earlier. The new document that Ying gave to me today will be ready on Monday.

If you have any questions, please call me at 650-624-1106.

Respectfully yours,

*Nicole Verona*

Nicole A. Verona  
Rigel Pharmaceuticals, Inc.

# Exhibit F 09/843,149

## DOCKETING/BILLING SYSTEM FILE INFORMATION (Patent/Design Patent)

Date: July 26, 1999

File No.: A-68292

Client: Rigel Pharmaceuticals

Access Code: 4931

Client

Attorney: DJB/RMS/DAV

Ref. No.:

New

Update

Close

Parent

Div.

CPA

CIP

### Subject Description

Title: TANKYRASEH, A Cell Cycle Protein

Inventors: Ying Luo

Serial No.:

Filing Date:

Patent No.:

Issue Date:

Assignee:

Related Files:

If Foreign file, please provide corresponding U.S. Serial Number  
or Patent Registration Number.

Misc. (Include any action items and due dates here!):

Submitted by: Gail Clark

Date: July 26, 1999

cc: Accounting

Docketing - Foreign

Docketing - US

Exhibit #G 09/843, 149

From: Nicole Verona <NVerona@rigel.com>  
To: "'dvance@flehr-iplaw.com'" <dvance@sfpo.fhtah.fleh...  
Date: 8/30/99 4:01pm  
Subject: FW: FW: info

Dear Dolly,

I forwarded your questions to Ying Luo and this is the response I received from him. I hope this helps. Also, I've got copies of the TNIK manuscript figures that you need. Would you like me to fax them to you?

Nicole

-----Original Message-----

From: Ying Luo [mailto:yluo@rigel.com]  
Sent: Sunday, August 29, 1999 2:44 PM  
To: Nicole Verona  
Subject: Re: FW: info

PAN is from PCNA screening. tankyraseH is from CIP screening. CIP is also called p21. R0101 has an entry in GenBank with full length sequence with a name called KIAA0101. No functional annotation about R0101. PPS was cloned and published before. The novelty is we can link PPS to RAD9, a cell cycle checkpoint control protein. You should have all figures of TNIK manuscript already. TNIK nucleotide sequences are attached. PAN nucleotide sequence is already in Genbank.

7868

Ying

At 03:21 PM 8/26/99 -0700, you wrote:

>Hi Ying!  
>  
>Here are some of the questions I need to discuss with you.

>  
>Nicole

>-----Original Message-----

>From: Dolly Vance [mailto:dvance@flehr-iplaw.com]  
>Sent: Friday, August 20, 1999 1:42 PM  
>To: nverona@rigel.com  
>Subject: info  
>  
>  
>Dear Nicole,  
>Hope you're well. Here's a complete list of what I am missing from the  
>initial 9 disclosures.  
>  
>1) The names of binding partners (if any actual) for CAH and  
>tankyraseH.  
>2) The nucleic acid and amino acid sequences for PAN and TNIK  
>(actually, all figures that go with the manuscript for TNIK).  
>3) Please confirm that R0101 and PPS are NOT novel, and that all  
>others are novel.

>  
>Thanks. Dolly

>P.S. I understand your hours are reduced. Any chance you can give me a  
>time frame for providing the above information? Thanks again, Dolly

>

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September 30, 1999

Ms. Dolly Vance  
Flehr, Hohbach, Test, Albritton and Herbert LLP  
4 Embarcadero Center, Suite 3400  
San Francisco, California 94111-4187

Dear Dolly,

Enclosed are documents pertaining to the cell-cycle patent applications that you requested.

The documents include:

1. TankyraseH abstracts involving TRF, P21, and PARP
2. TankyraseH nucleotide sequence alignment report
3. TankyraseH amino acid sequence alignment report
4. R0101 figures with corrected CDK 2, 3, and 4 labels
5. Mkinase nucleotide and amino acid sequences with its kinase domain and nuclear localization sequence (NLS) highlighted

Additional information will be sent to you next week.

Please call or email me if you have any questions.

Sincerely,

*Nicole Verona*

Nicole Verona

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